IN THE CLAIMS:

Please cancel claims 15-17 and 20-28 without prejudice.

Please amend claims 1, 3, 4, 6, and 8-11 as follows:

C1

1. (Three times amended) A method of detecting a splicing defect in a human dihydropyrimidine dehydrogenase gene, comprising determining whether the residue of a human genomic DNA encoding the human dihydropyrimidine dehydrogenase gene at the position indicated as nucleotide 434 of SEQ ID NO: 1 is a G residue or determining whether the residue at the position indicated as nucleotide 434 of SEQ ID NO: 1 is an A residue, wherein the substitution of the G residue with an A residue at position 434 causes the splicing defect in the human dihydropyrimidine dehydrogenase gene; and wherein the DNA, other than for any substitution of the G residue at position 434, comprises a nucleotide sequence identical to the sequence of residues 432-435 of SEQ ID NO: 1.

3. (Three times amended) The method of claim 2, wherein the method comprises amplifying the genomic DNA with a polymerase chain reaction primer from about 15 to about 20 nucleotides long and wherein the nucleotides are in a sequence complementary to a sequence of SEQ ID NO: 1 located between position 434 and 861.

C2

4. (Three times amended) The method of claim 2, wherein the detecting is by digestion of the amplified DNA with a Mae II restriction endonuclease.

C3

6. (Three times amended) A method of screening human patients for sensitivity to 5-fluorouracil, comprising isolating a genomic DNA from the patient, wherein the DNA comprises positions 432-435 of SEQ ID NO: 1; and determining whether a G residue is the nucleotide at position 434, and wherein the DNA, other than for any substitution of the G residue at position 434, comprises a nucleotide sequence identical to the sequence of residues 432-435 of SEQ ID NO: 1.

8. (Three times amended) The method of claim 7, wherein the method comprises amplifying the genomic DNA with a polymerase chain reaction primer from about 15 to about 20 nucleotides long and wherein the nucleotides are in a sequence complementary to a sequence of SEQ ID NO: 1 located between position 434 and 861.

9. (Three times amended) The method of claim 7, wherein the determining is by digestion of the amplified DNA with a Mae II restriction endonuclease.

C4

10. (Three times amended) A composition comprising a polymerase chain reaction primer from about 15 to about 20 nucleotides long wherein the nucleotide sequence is complementary to a nucleotide sequence of SEQ ID NO: 1 located between position 434 and position 861.

11. (Three times amended) The composition of claim 10, wherein the nucleotides are in a sequence corresponding to a sequence of SEQ ID NO: 1 located between position 434 and position 534.

REMARKS

Claims 1-11 are pending and presented for examination. Claims 1, 3, 4, 6, and 8-11 are amended. Claims 15-17 and 20-28 are cancelled.

Claims 1-5, 8, 10, 11, 15, 20, 22, 24 and 26 stand rejected under 35 U.S.C. §112, 2nd paragraph as allegedly indefinite for failing to distinctly point out and claim the subject matter the Applicants regard as their invention.

Claims 1-4, 8-10, 15-17, 20, 22 24, 26, and 27 stand rejected under 35 U.S.C. §112, first paragraph as allegedly not satisfying the written description requirement.

Claims 4, 9, 17, and 27 stand rejected under 35 U.S.C. §112, first paragraph as allegedly not enabled.

Claims 10, 11, 15, and 24 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Gonzalez et al. in view of Meinsma et al.

Applicants respond to each of the above rejections below.